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STUDIES ON PULMONARY MECHANICS
IN INFANTS

BY HANS AHLSTRÖM

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The present thesis is based on the following papers:

- (I) Pulmonary mechanics in infants. Methodological aspects. Scand. J. Resp. Dis. Accepted for publication. Together with B. Jonson.
- (II) Pulmonary mechanics during the first year of life. Scand. J. Resp. Dis. Accepted for publication. Together with B. Jonson.
- (III) Pulmonary mechanics in infants surviving severe neonatal respiratory insufficiency. Acta Paediat. Scand. Accepted for publication.

In the text these papers will be quoted as I, II and III.

ABBREVIATIONS

Pulmonary mechanical properties

V_T	= tidal volume
$\dot{V}_{IE}$	= minute ventilation
$\dot{V}$	= air flow rate
Cdyn (l)	= dynamic compliance of the lungs
Rf (l)	= functional lung resistance
Gf (l)	= functional lung conductance
FRC	= functional residual volume

Diseases and means of treatment

IRDS	= idiopathic respiratory distress syndrome
VSD	= ventricular septal defect
PDA	= patent ductus arteriosus
CPAP	= continuous positive airway pressure
IPPV	= intermittent positive pressure ventilation

INTRODUCTION

Besides physical and radiological examination of the chest arterial blood gas analysis is the most important source of diagnostic information about pulmonary disease in infants, making it possible to judge to what extent the lungs fulfil their task as gas exchangers. Decreased arterial oxygen tension and increased carbon dioxide tension indicate pulmonary malfunction but tell us little about its nature. Furthermore, pulmonary malfunction during infancy may not be discovered by either physical, radiological or blood gas examinations. For more specific and detailed information of pulmonary disease other investigations must be made. Among these, measurements of the mechanical properties of the lungs can give important information concerning some of the conditions necessary for an efficient gas exchange.

Special problems are connected with measurements of pulmonary mechanics in infants since they cannot co-operate and all investigations must be performed during spontaneous breathing at sleep (28, 36).

Several methods for investigations of pulmonary mechanics in infants are described earlier (8, 9, 22, 24, 25, 33, 48), but most methods are designed for newborn infants. These methods cannot be used in older infants, without considerable modifications including sedation. Sedation is apt to produce unphysiological conditions and may even be dangerous in infants with pulmonary disease. The forced oscillatory method (48) can be used without sedation after the neonatal period. This method gives a measure of the resistance of the lungs and the thoracic and abdominal wall, but no specific information on pulmonary compliance.

The results obtained are therefore somewhat difficult to interpret and they are not fully comparable with the usual measurements of pulmonary mechanics.

Earlier described methods including measurements of the oesophageal pressure are time-consuming and can hardly be used as routine procedures. Great experience is needed in the choice of "representative breaths" for manual calculations of pulmonary mechanics. These methods have therefore been used mainly for scientific purposes.

A method for investigation of mechanical properties of the lungs must first of all be non-hazardous. It should serve several purposes:

- 1) As a diagnostic tool in the investigation of even severely ill infants, with different types of pulmonary disease.
- 2) For the follow-up of infants who had severe pulmonary disease during the neonatal period.
- 3) For evaluations of the effect of surgical or pharmacological therapeutical procedures.
- 4) For scientific purposes e.g. to provide a better understanding of the pulmonary physiology of the normal infant and the infant with pulmonary disease.

A new method for studies of pulmonary mechanics in infants is presented (1), which attempts to solve some of the specific methodological problems connected with investigations of infants *after* the neonatal period. Several of these problems will be discussed here. Different applications of the method will be described. The method has been found convenient enough to be used in clinical routine.

METHODOLOGICAL PROBLEMS

1. Security considerations

A method designed for clinical use in the investigation of infants, who may be critically ill in ventilatory insufficiency, must not involve risks of deterioration of the condition. If the ventilatory reserves are small, procedures leading to decreased ventilatory ability are potentially hazardous. It is naturally of utmost importance that all risks are considered, when a new method for investigation of pulmonary mechanics is introduced. The need for gentle handling and great patience in the investigation of infants is wellknown to every pediatrician.

A prerequisite for proper evaluation of pulmonary mechanics in infants is that the investigation is performed at rest and preferably at sleep (28, 36). To achieve this, sedatives have been used in all previous studies, including measurements of the oesophageal pressure in infants after the neonatal period (9, 24, 33). Sedatives were avoided in the present study for two main reasons:

- 1) Most sedatives have a depressive effect on the respiration, which is obviously hazardous in the investigation of infants with ventilatory insufficiency.
- 2) Sedatives may influence the breathing and the information on pulmonary mechanics would then be "unphysiological" (36).

If the infants have been deprived of sleep for 2–7 hours and newly fed the investigation can be performed on the sleeping infant without the use of sedatives if suitable equipment for measurements of oesophageal pressure and air flow rate is used (I). Feeding does not have any adverse effect on the respiratory mechanics in newborn infants (40).

In most previous measurements of oesophageal pressure in infants balloon catheters have been used. After several trials we abandoned the use of

balloon catheters in favour of fluid filled catheters (I). In non-sedated infants it was found that a thin polyethylene catheter was more suitable than a balloon catheter, which is inevitably coarser and more rigid. The catheter was easily introduced through the nose without much irritation of the infant. Local anaesthesia of the mucous membranes of the nose or the pharynx was not necessary. This is advantageous since local anaesthesia of the upper airways increases the risk of aspiration. As the infants were newly fed the risk of vomiting must be considered even with the thin oesophageal catheter used.

Vomiting in an infant in supine position with the face fixed in a sealing diaphragm may be dangerous, especially in infants with respiratory distress. The described body plethysmograph for measurement of air flow rate (I) is constructed so that an infant can be taken out of it, within a few seconds if vomiting or other complications should occur. Equipment for suction, oxygen administration, and positive pressure ventilation should be close at hand during the investigation. A physician trained in the care of sick infants must be present throughout the investigation.

During our preliminary studies with a balloon catheter vomiting occurred several times, whereas in about 200 investigations with a fluid filled catheter, only one infant (with gastro-enteritis) vomited.

Infants with *severe* ventilatory insufficiency cannot be transported to a laboratory for examination without considerable risks of deterioration of the condition. A modification of the described method for studies of pulmonary mechanics makes examination of these infants possible. A face chamber, originally made for the treatment of infants with idiopathic respiratory distress syndrome (1) was used (fig. 1). This is a cylinder with a sealing diaphragm of the same model as the one

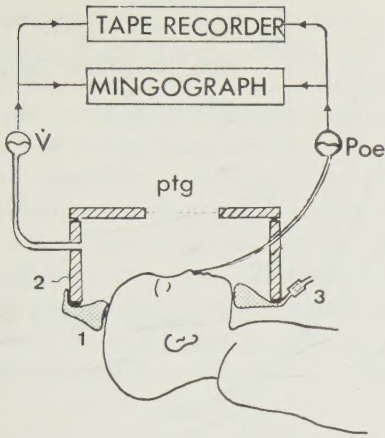


Fig. 1. Equipment for bedside studies of pulmonary mechanics with a face chamber. V and Poe indicate transducers for pressure and flow measurements. Ptg indicates the pneumotachograph screen in the lid of the face chamber. The face chamber is placed around the sealing diaphragm, 1, attached to the cylindrical face chamber, 2. The air is evacuated from the sealing diaphragm through the tube, 3.

used in the body plethysmograph. In the lid of the cylinder a pneumotachograph screen was mounted. The face chamber was attached to a stage with the infant's face protruding through the sealing diaphragm into the face chamber. An oesophageal catheter was gently introduced and passed out through the face chamber and connected to the pressure transducer. The signals for oesophageal pressure and air flow rate were fed to a tape recorder (Analog 7, Philips) and a direct writing recorder (Mingograph 81, Siemens-Elema). Instead of using carbon dioxide for hyperventilation, which was considered risky, the infants were rebreathing dead space air of the face chamber for about two minutes. After the investigation the tape recorded data were analyzed by the computer as in the original method (I).

As this equipment for measurements of air flow rate does not measure compression and decompression of gas within the thorax the obtained values are not exactly comparable to normal data obtained with the original method. They seem, however, sufficient for an evaluation of the pulmonary properties in severely ill infants. An example will be given of the investigation of an infant with severe respiratory insufficiency (page 16).

In the studies of newborn infants, who are kept in incubators, investigation with the face chamber method seems to be the most suitable. An optimal

environment with respect to temperature and humidity will be better provided within an incubator than in the body plethysmograph.

2. Standardization procedures

In the investigation of pulmonary mechanics in adults, voluntary hyperventilation, special breathing patterns such as panting, and regulation of air flow rate are examples of ways to standardize the breathing pattern. Obtained values of compliance are related to the lung volume, resistance to the airflow and so on. In infants these procedures are not possible and other forms of standardization of the procedure must be made to obtain reliable and reproducible values of pulmonary mechanics.

For adequate comparisons between different infants and between one and the same infant investigated on different occasions, standardized conditions of the examinations are necessary. During *sleep* rather basal conditions in most infants can be assumed. However, it is difficult to evaluate the depth of the sleep of an infant during the investigation. High breathing frequency at rest may be a sign of excitation. In most normal infants a moderate increase of the breathing frequency was seen at increasing minute ventilation during carbon dioxide hyperventilation. In some infants *decreasing* breathing frequency was found during carbon dioxide exposure and a further decrease in frequency occurred after the cessation of carbon dioxide. This pattern may indicate that basal conditions were not present at the beginning of the investigation.

In a non-sedated infant the equipment must not disturb the infant's sleep. It appears that the infants are very sensitive to any tactile stimulus on the area around the nose and the mouth. The sealing diaphragm of the body plethysmograph does not press on the infant's face. One important factor for the comfort of the infants is that the plethysmograph is air conditioned with respect to temperature and humidity. The investigations were performed in semidarkness.

The use of *nose drops* did not significantly change pulmonary mechanics in normal infants (I), but may contribute to the standardization in reducing the nasal resistance particularly in infants with respiratory infections. The concentration of the nose drops (oxymetazolin 0.1 mg/ml, Nezeril®) was so low that any effects on the bronchi

and the central nervous system could be excluded (17).

Studies in adults have shown that *hyperventilation* is one way of standardizing the breathing pattern (12, 29). During carbon dioxide induced hyperventilation a closer correlation of $C_{dyn}(I)$ and $\log Gf(I)$ to body size measures was found than at rest in studies of normal infants (II). This makes the use of data obtained at hyperventilation preferable.

In some infants, especially those prematurely born, the breathing is irregular with repeated short periods of apnoea — "periodic breathing". Measurement at rest is sometimes not possible in these infants (III). After exposition to 5 per cent carbon dioxide in oxygen the breathing became regular within one minute. This regularization of breathing may be due to both the increased carbon dioxide concentration and the high oxygen content in the inspired gas (7, 11, 23).

In most previous studies on pulmonary mechanics during infancy the calculations have been made manually from recordings of pressure, volume, and flow. The use of *computerized calculations* has several advantages. The calculations are *free from bias*. The large amount of primary information included in one recording makes the measurements *less sensitive to variations in the breathing pattern* (I). The results are immediately available, which is of importance in the diagnostic use of the method.

3. Sources of errors in the measurement of pulmonary mechanics in infants

In infants, lung compliance must be measured during dynamic conditions, since the infants cannot hold their breath.

$C_{dyn}(I) = V_T/\Delta P$, where $C_{dyn}(I)$ is dynamic compliance, V_T the tidal volume and ΔP is the pressure change between the moments when the airflow is zero before and after every inspiration. It is obvious that one prerequisite for correct measurement of $C_{dyn}(I)$ is that the pressure and flow signals are recorded *without phase shift*. The equipment used in the present study was carefully controlled in this respect (I). Even small phase shifts between flow and pressure were found to cause considerable errors in the obtained values of $C_{dyn}(I)$ especially in infants with a high breathing frequency and high pulmonary resistance (fig. 2).

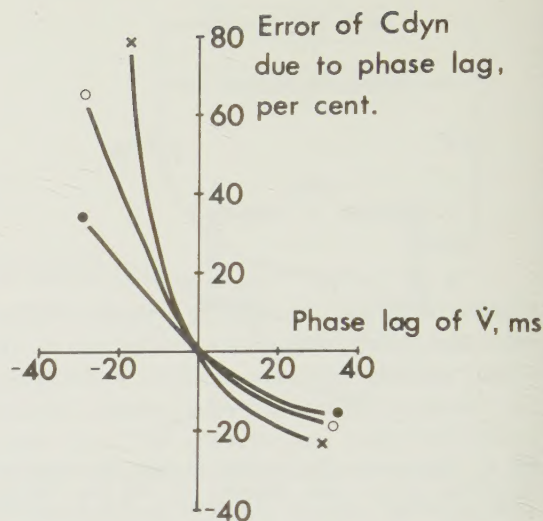


Fig. 2. Errors caused by phase lag in values of $C_{dyn}(I)$ in per cent of true values. Positive values on abscissa means that flow rate, $\dot{V}$, lags behind pressure.

- normal infant, $Rf(I)$ 21.7 cm H_2O / (l/s), 47 breaths/min.
- infant with obstructive bronchitis, $Rf(I)$ 108 cm H_2O / (l/s), 33 breaths/min.
- x infants with ventricular septal defect, $Rf(I)$ 46.4 cm H_2O / (l/s), 141 breaths/min.

Small airbubbles within the catheter and the transducer may cause considerable phase shifts. When using a fluid filled system for the pressure recording, free air will be released at body temperature from the fluid, if this is saturated with air at room temperature. Repeated flushing may even increase the amount of air released from the fluid. The frequency response of such a system will be very variable and it is obviously not possible to compensate for this phase lag e.g. by electrical means. By using *boiled water* the problems of dissolved air is eliminated. In fact, air adhering to the walls of the catheter will rather be dissolved. The catheter-transducer system must be carefully flushed before the investigation and repeatedly during it, to prevent the holes of the tip of the catheter to be occluded by the oesophageal wall or mucus.

According to Senterre and Guebelle (41) fluid filled catheters are unsuitable in the measurements of the oesophageal pressure because of the *great amplitude variations* at different frequencies. Their recording system was obviously not suitable. With the equipment used in this work a correct response could be obtained up to 60 Hertz. The signals were

electrically damped to give the same frequency response as the body plethysmograph.

The recording from a body plethysmograph is sensitive to *transient pressure variations* in the room. The compensation chamber (42) connected to the transducer eliminates these errors. The compensation chamber is connected to the secondary side of the transducer and is open to the room via a screen pneumotachograph. The volume of the compensation chamber is adjusted to give the same time constant as that of the body plethysmograph.

Leaks in the body plethysmograph give false values of the volume and flow recordings. The tightness of the body plethysmograph used was tested by feeding a known airflow into it, first without an infant when the hole for the infant's face was covered by a lid, and later during the actual investigation with the infant in proper position. The resulting signals should be the same if the system was tight.

STUDIES OF PULMONARY MECHANICS IN NORMAL INFANTS

26 infants without heart and lung diseases were studied (II). Data of V_T , $\dot{V}_{IE}$, $C_{dyn}(l)$, and $Gf(l)$ were closely correlated to body size measures. Generally our data were in agreement with those of other authors (9, 24, 33, 48). Correlation to height was found suitable in comparisons with sick infants (II, III). From the formula for linear

regression the expected values for some properties of pulmonary mechanics from infants between 40 and 75 cm are calculated (Table 1). As the equation for regression between $Gf(l)$ and height is logarithmic (II) the values of ± 1 and 2 SD are given, to allow easy estimate of the conductance values of an infant.

Table 1. *Mechanical properties of the lungs related to height.*

Height cm	V_T ml	$\dot{V}_{IE}$ l/min	$C_{dyn}(l)$ ml/cm H ₂ O	$Gf(l)$ (l/s)/cm H ₂ O				
				-2 SD	-1 SD	mean	+1 SD	+2 SD
40	8.5	0.68	4.2	0.010	0.014	0.019	0.027	0.037
41	10.0	0.72	4.4	0.010	0.014	0.020	0.028	0.039
42	11.5	0.76	4.5	0.011	0.015	0.021	0.029	0.040
43	13.0	0.80	4.6	0.011	0.015	0.021	0.029	0.041
44	14.5	0.84	4.8	0.011	0.016	0.022	0.030	0.042
45	16.0	0.88	4.9	0.012	0.016	0.022	0.031	0.043
46	17.5	0.92	5.1	0.012	0.016	0.023	0.032	0.044
47	19.0	0.96	5.2	0.012	0.017	0.024	0.033	0.045
48	20.4	1.00	5.4	0.013	0.017	0.024	0.034	0.047
49	21.9	1.04	5.5	0.013	0.018	0.025	0.035	0.048
50	23.4	1.08	5.7	0.013	0.018	0.026	0.036	0.049
51	24.9	1.12	5.8	0.014	0.019	0.026	0.037	0.051
52	26.4	1.16	6.0	0.014	0.019	0.027	0.038	0.052
53	27.9	1.20	6.1	0.014	0.020	0.028	0.039	0.054
54	29.4	1.24	6.3	0.015	0.021	0.029	0.040	0.055
55	30.9	1.28	6.4	0.015	0.021	0.029	0.041	0.057
56	32.4	1.32	6.5	0.016	0.022	0.030	0.042	0.058
57	33.9	1.36	6.7	0.016	0.022	0.031	0.043	0.060
58	35.4	1.40	6.8	0.017	0.023	0.032	0.044	0.062
59	36.9	1.44	7.0	0.017	0.024	0.033	0.046	0.063
60	38.4	1.48	7.1	0.017	0.024	0.034	0.047	0.065
61	39.9	1.52	7.3	0.018	0.025	0.035	0.048	0.067
62	41.4	1.56	7.4	0.018	0.026	0.036	0.050	0.069
63	42.9	1.61	7.6	0.019	0.026	0.037	0.051	0.071
64	44.3	1.65	7.7	0.019	0.027	0.038	0.052	0.073
65	45.8	1.69	7.9	0.020	0.028	0.039	0.054	0.075
66	47.3	1.73	8.0	0.021	0.029	0.040	0.055	0.077
67	48.8	1.77	8.2	0.021	0.029	0.041	0.057	0.079
68	50.3	1.81	8.3	0.022	0.030	0.042	0.058	0.081
69	51.8	1.85	8.4	0.022	0.031	0.043	0.060	0.084
70	53.3	1.89	8.6	0.023	0.032	0.044	0.062	0.086
71	54.8	1.93	8.7	0.024	0.033	0.046	0.064	0.088
72	56.3	1.97	8.9	0.024	0.034	0.047	0.065	0.091
73	57.8	2.01	9.0	0.025	0.035	0.048	0.067	0.093
74	59.3	2.05	9.2	0.026	0.036	0.050	0.069	0.096
75	60.8	2.09	9.3	0.026	0.037	0.051	0.071	0.099

SD: ± 7.8 ± 0.3 ± 1.6

It could be suspected that pulmonary properties such as compliance and conductance would not be a linear function of the *height*, but rather vary *exponentially*, e.g. with height^3 , i.e. a volume measure. However, in this sample of normal infants the closest correlations were found to the more primary measurements. It must, however, be stressed that these calculations are based upon measurements of infants, who generally were below 70 cm. In higher infants correlations to exponential functions of body size measures may

be better (II). This may explain why some other authors (9, 33) have found higher values of e.g. V_T , $\dot{V}_{IE}$, and $C_{dyn}(l)$ in some large infants than would be expected from our data. In the studies of infants recovering from severe neonatal ventilatory insufficiency (III), some values of e.g. $C_{dyn}(l)$ in large infants were higher than expected in relation to the normal values, presented in paper II. This thus does not necessarily mean that these infants have abnormal elastic properties of the lungs (see page 14).

STUDIES OF PULMONARY MECHANICS IN DISEASED INFANTS

1. Interpretation of data from diseased infants

Recording of the *breathing frequency* is probably the most used simple test in evaluating diseases of the chest in infants. Tachypnoea occurs both in obstructive airway disease and conditions characterized by a low pulmonary compliance. Increasing breathing frequency may also be a valuable sign of deterioration of the infant's condition. The value of recording the breathing frequency repeatedly in diseased infants is thus indisputable. However, isolated values of the breathing frequency e.g. obtained during measurements of pulmonary mechanics are of minor value. Also normal infants without heart or lung disease could occasionally have a high breathing frequency even during sleep (I). Similar results are reported by other authors studying pulmonary mechanics in infancy (24, 33).

Data on *tidal volume* and *minute ventilation* seem to give little, if any, information in the evaluation of pulmonary function in hitherto studied groups of patients. Attempts to obtain reproducible values of thoracic gas volume (e.g. FRC) failed (I) as a non-sedated infant immediately wakes up and moves when the mouth and nose are occluded. Other authors, who have studied thoracic gas volume in infants after the neonatal period have been forced to use more or less heavy sedation (9, 33).

Studies of *Cdyn(I)* have proved to give valuable information on the mechanical properties of the lungs (III). However, the interpretation of the values of *Cdyn(I)* in diseased infants is sometimes difficult. A low value of *Cdyn(I)* does not mean that the lungs are abnormally stiff if the airways are obstructed (III). It is known that such a decreased value of *Cdyn(I)* occurs in obstructive lung disease, particularly at *high breathing frequencies*. This phenomenon of frequency dependent compliance has been thoroughly analysed by Otis et al. (32). If some airways close because of airway disease the values of *Cdyn(I)* may further decrease (21).

During infancy many diseases give an increased pulmonary resistance. Measurements of *pulmonary resistance* or *conductance* may thus be of importance in the evaluation of the lung function in infants with cardio-pulmonary diseases. The *functional resistance* is calculated from the measured work rate against the pulmonary resistance and the ventilation (20, II). This work comprises work associated with flow in and out through the lungs, and work to overcome tissue viscosity. Roughly similar values of *Rf(I)* are obtained at varying ventilation (I). This independency of ventilation makes *Rf(I)* particularly useful as it allows comparisons between observations at different ventilation volumes.

In most infants the obtained values of *Rf(I)* or *Gf(I)* are sufficient for an adequate evaluation of the patency of the airway. If either of these values is abnormal additional information may be obtained from studies of the form of pressure-flow or pressure-volume loops (13, 19, I). Thus a pressure-flow loop may show e.g. high resistance at the end of the inspiration, which may indicate an extrathoracic airway obstruction (III). Several authors have used the pressure-flow loops for actual measurements of e.g. inspiratory and expiratory resistance, assuming that the elastic recoil pressure has a linear relation to the lung volume. This is not reasonable in infants with pulmonary disease (I). From the pressure-flow loops the resistance values at zero flow can also be calculated (I). This is done under the assumption that the pressures associated with inertia of the lungs and airway gas are so small that they can be disregarded (22, 35, 36). The zero resistance values give principally information on the patency of the airways at zero flow i.e. during "static conditions" (I). Together with the computer calculated values, these zero flow resistance values make it possible to compare different infants numerically. Numerical values are also useful in follow-up studies.

2. Studies of pulmonary mechanics after neonatal respiratory insufficiency

The use of intermittent positive pressure ventilation (IPPV) and continuous positive airway pressure (CPAP) in the treatment of ventilatory insufficiency in the neonatal period has increased the survival rate dramatically. Some survivors have, however, pulmonary symptoms for a long time after the cessation of the ventilatory support. Several authors have discussed the reasons for these symptoms (3, 4, 27, 30, 31, 38, 44, 45) but few studies of the pulmonary function have been made (2, 10, 43).

Ventilators for IPPV have been used in the neonatal unit in Lund since 1969. After the encouraging report by Gregory et al. (14) concerning treatment of idiopathic respiratory distress syndrome (IRDS) with CPAP this method was introduced.

The use of an indwelling tracheal tube has several disadvantages:

- 1) The tube may damage the mucous membranes in the upper airways resulting in decreased ciliary function and stagnation of mucus in the airways (39).
- 2) The risk of pulmonary infection is increased.
- 3) The tube can suddenly be occluded by mucus.
- 4) Endotracheal tubes seem to be a prerequisite for the development of bronchopulmonary dysplasia (44).

Because of these potential hazards CPAP treatment via an endotracheal tube seems justifiable only in infants with *severe* ventilatory insufficiency due to IRDS. The risk of apnoea and secondary intracranial ischaemic damages is in these infants considerably increased.

The "grunting" phenomenon seen in infants with IRDS, may be regarded as an attempt to prevent alveolar collapse at the start of every expiration, by elevating the transpulmonary pressure (16). The ability of grunting is lost when the infant is intubated. If the continuous positive pressure accidentally decreases the risk of severe deterioration in the condition of the intubated infant is considerable. This is a further argument against intubation.

The head chamber suggested by Gregory et al. (14) for CPAP-treatment without intubation was

not found suitable because of the risk of congestion of the veins of the neck, which has been found hazardous (46). Furthermore, the head chamber provides poor access to the upper airways in emergencies. The risk of cochlear damage because of the noise level in a head chamber must also be considered (5).

The *face chamber* described earlier (page 6) was constructed. Because of the good results in the treatment of IRDS with this device (1), the use of IPPV in IRDS was abandoned in our neonatal unit, except for those occasions when the infants have sudden apnoeic spells. In ventilatory insufficiency due to postasphyxia syndrome and respiratory insufficiency syndrome, IPPV is still the therapy of choice. In the facilitation of weaning from IPPV in these infants, and to shorten the time of IPPV, CPAP via a face chamber is also very convenient.

A prospective survey of pulmonary mechanics of 24 infants surviving three types of ventilatory insufficiency was made (III).

- 1) 15 infants had *idiopathic respiratory distress syndrome*. The diagnosis was based upon clinical criteria (i.e. grunting, retractions and tachypnoea) and a $P_{aO_2} < 70$ mm Hg when breathing 100 per cent oxygen (hyperoxia test). A radiological reticulogranular picture was considered as supportive for the diagnosis.
- 2) 6 infants had recurrent apnoea in the prematurity (*respiratory insufficiency syndrome*). This syndrome is chiefly seen in small prematures, with an apparently normal lung function during the first day(s) of life. Apnoeic spells with bradycardia, possible due to cerebral immaturity makes ventilatory support necessary.
- 3) 3 infants suffered from the *postasphyxia syndrome* (37), which is seen in fullterm as well as in preterm infants. The ventilatory insufficiency is due to an intrauterine asphyxia often in combination with aspiration of amniotic fluid. Due to hypoxia and acidosis the normal adjustment of the circulation after birth will be impaired with subsequent right-to-left shunting of the blood either in the lungs or via a patent ductus arteriosus. At hyperoxia test a poor increase of P_{aO_2} is found.

In follow-up studies of 20 of the 24 infants surviving severe neonatal ventilatory insufficiency

it was found that early measurement of pulmonary conductance was a valuable tool for prognostic evaluation as concerns pulmonary symptoms later during infancy. A valid comparison of the different treatments could not be made since the groups with IRDS were not comparable, as to the severity of the disease (III). However, no infant treated with CPAP via a face chamber had any clinical pulmonary sequelae at the follow up studies. IPPV treatment of long duration (i.e. > 200 hours) was associated with low values of $C_{dyn}(l)$ and $G_f(l)$ at the initial investigation. Most infants IPPV treated for long periods of time later developed clinical respiratory symptoms. One infant CPAP-treated via an endotracheal tube and breathing high oxygen concentration for several days had gross pulmonary abnormalities and clinical symptoms during the first year of life, suggesting bronchopulmonary dysplasia.

Independent of diagnosis and way of treatment a general trend towards low $G_f(l)$ in relation to height was found at the follow-up studies. Bronchospasm, increased susceptibility to airway infection due to the prematurity, or true sequelae from the primary disease may all contribute to this tendency towards airway obstruction.

The high values of $C_{dyn}(l)$ at the reinvestigations in infants higher than 60 cm do not necessarily indicate pulmonary malfunction (see page 11). In fact, when comparing $C_{dyn}(l)$ of normal infants (II) higher than 60 cm with those of corresponding height in this investigation no statistically significant difference was found.

The method described for measurements of pulmonary mechanics was found very suitable for this type of study. Information of prognostic value is obtained and comparisons between different therapeutical approaches to pulmonary diseases and their effect on pulmonary mechanics can be made in the future.

3. Studies of pulmonary mechanics in infants with cardio-vascular left-to-right shunts

Some of the main features in the clinical picture of infants with congestive heart failure are of respiratory nature. Thus tachypnoea and sternal and intercostal retractions are dominating symptoms especially in infants with a left-to-right shunt via a ventricular septal defect (VSD) or a patent ductus arteriosus (PDA). These symptoms can be sup-

posed to be correlated to the magnitude of the shunt as well as to the pressures in the pulmonary circulation. In addition these infants have an increased susceptibility to airway infections which sometimes may lead to severe obstructive symptoms.

It can be assumed that any disturbance of the heart function and the intrapulmonary circulation disturbs the mechanical properties of the lungs to a certain extent. In adults with cardiac disease many studies of pulmonary mechanics have been performed but few investigations have been done on infants (15, 18, 47). The presented method for measurement of pulmonary mechanics was found suitable for investigation of infants with congenital heart defects. To illustrate this use of the method some preliminary results will be given.

19 infants with cardio-vascular left-to-right shunts, verified by cardiac catheterisation were studied. 4 infants had PDA and 15 VSD. Pulmonary artery pressure was increased, mostly due to the increased blood flow. The pulmonary vascular resistance was normal in 18 and slightly elevated in one infant. Pulmonary mechanics were measured just before or after the time of the cardiac catheterisation and several infants were reinvestigated at one or more occasions during the first year of life. All infants with PDA were operated on and pulmonary mechanics was reinvestigated. The absence of cardiac murmurs and a decreasing roentgenological heart volume were taken as reliable signs of a successful operation.

In agreement with other authors (15, 18, 47) it was found that $C_{dyn}(l)$ generally was decreased compared to normal infants (fig. 3). Though the infants with left-to-right shunts as a group had significantly lower values of $C_{dyn}(l)$ than expected ($p < 0.001$), 9 of them had values within the normal range. Out of these, two infants with large shunts but with a moderate increase of the pulmonary artery pressure had higher values of $C_{dyn}(l)$ than predicted.

A significant correlation between the reduction in $C_{dyn}(l)$ and the mean pulmonary artery pressure was found (fig. 4). Wallgren et al. (47) and Howlett (18), who have investigated pulmonary mechanics in infants with various types of congenital heart defects were not able to find such a correlation. Griffin et al. (15), who studied infants with isolated VSD and PDA found a significant

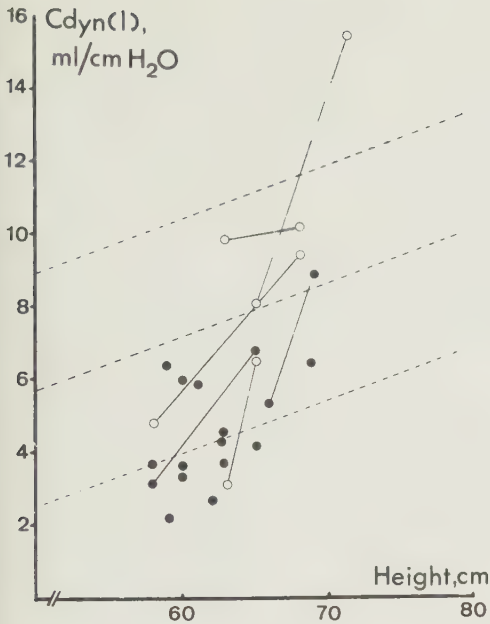


Fig. 3. $C_{dyn}(I)$ in relation to height. The dotted lines indicate the expected value ± 2 SD (II). Values before and after closure of a PDA or pulmonary banding in VSD, are connected with lines.

● ventricular septal defect.
○ patent ductus arteriosus.

correlation between the peak pulmonary artery pressure and $C_{dyn}(I)$. They suggested that serial measurements of pulmonary compliance in infants with congenital heart defects could give important prognostic information. The results from serial measurements in the present study do not confirm this suggestion. Clinical improvements or deteriorations were not significantly correlated to changes in $C_{dyn}(I)$.

After closure of PDA a significant increase of $C_{dyn}(I)$ was found in three of the four investigated infants (fig. 3). In three infants with VSD pulmonary banding was performed because of repeated severe obstructive airway disease in combination with pulmonary hypertension and congestive heart failure. One infant died. An increase of $C_{dyn}(I)$ was found in the other two (fig. 3).

In spite of the high incidence of obstructive airway disease in infants with large left-to-right shunts and elevated pulmonary artery pressure the obtained values of $G_f(I)$ were in general not decreased. In fact, many infants even those with huge shunts and significant pulmonary hypertension had *higher* values of $G_f(I)$ than expected. In some infants the conductance values varied considerably during the investigation. The pressure-flow loops were generally normal with normal endexpiratory and endinspiratory resistance values.

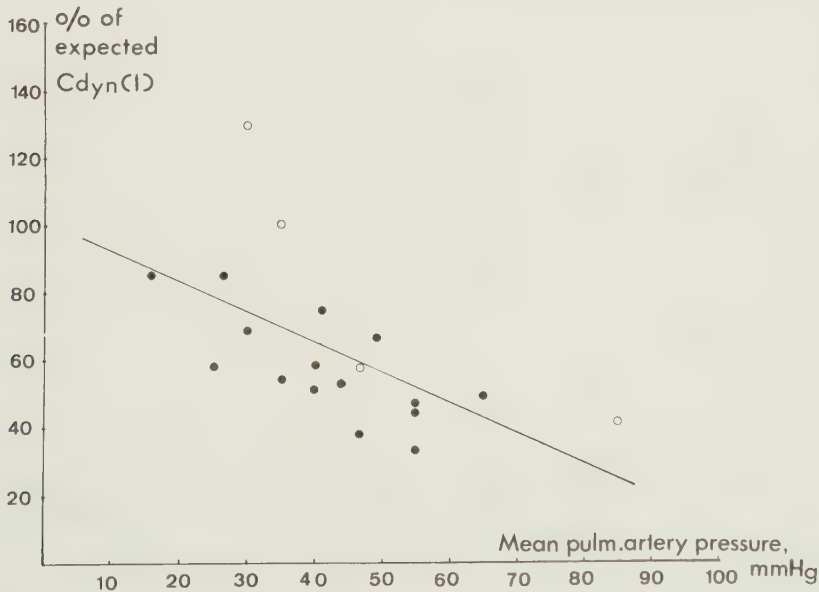


Fig. 4. Correlation between obtained values of $C_{dyn}(I)$ in per cent of the expected ones and mean pulmonary artery pressure.

The regression line $y = 102.4 - 0.9x$ is drawn. The correlation is significant, $p < 0.01$; $r = 0.60$. Symbols: see fig. 3.

However, during manifest airway infection with bronchial obstruction the values of $Gf(l)$ decrease considerably. The previously low values of $Cdyn(l)$ decrease further and the infants may be critically ill in severe respiratory insufficiency.

Fig. 5 shows the pressure-flow loops from a 3 1/2 months old infant with VSD and a large left-to-right shunt and pulmonary hypertension. At the first investigation it had signs of congestive heart failure with tachypnoea, intercostal retractions and moderate liver enlargement. Measurement of pulmonary mechanics revealed an increased minute ventilation, a low $Cdyn(l)$ and a normal $Gf(l)$. During an airway infection one week later the infant's condition rapidly deteriorated. Reinvestigation of pulmonary mechanics was performed with the modified mobile equipment described above. A remarkable decrease of both the values of $Cdyn(l)$ and $Gf(l)$ was found. Due to severe pulmonary insufficiency the infant was treated with CPAP via a face chamber (1). A dramatic

improvement of the condition of the infant was found during spontaneous breathing against a continuous positive pressure of 6–8 cm H_2O . After one week of CPAP treatment the infant was referred to the clinic of thoracic surgery for pulmonary banding. Unfortunately the infant died two weeks later due to postoperative complications.

As all data of the infants with cardiac left-to-right shunts are not yet completely analyzed, the reasons for the changes in the pulmonary mechanics in these infants can at the present not be fully discussed. Obviously the combination of a decrease of $Gf(l)$ during airway obstruction e.g. due to infections, associated with a further decrease of $Cdyn(l)$ gives rise to an enormous increase of the work of breathing. The risk of severe deterioration and respiratory and circulatory insufficiency is considerable. It is well known that infants with large left-to-right shunts may need IPPV and/or urgent surgical intervention to combat congestive

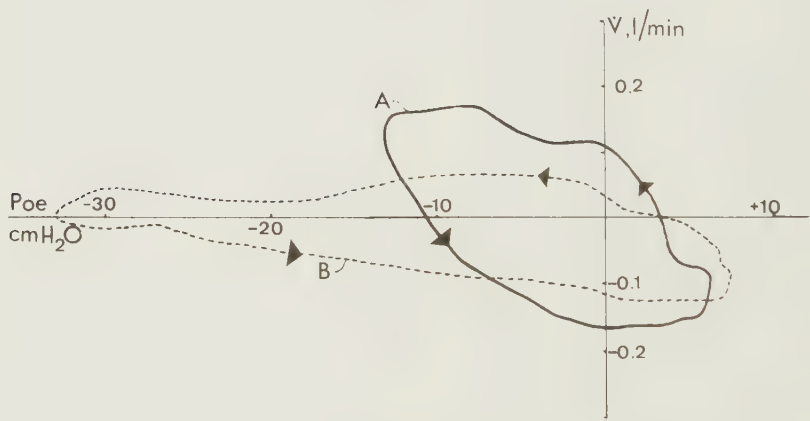


Fig. 5. Pressure-flow loops in an infant with VSD and pulmonary hypertension. The loops run counterclockwise indicated by arrows. Positive flow values: inspiration. Loop A is obtained at the initial investigation during moderate congestive heart failure and is apart from a low $Cdyn(l)$ normal. Loop B is obtained at the reinvestigation during ventilatory insufficiency 10 days later during an airway infection. There are excessive respiratory varia-

tions in the oesophageal pressure, reflecting low $Gf(l)$ and $Cdyn(l)$ values.

	$Cdyn(l)$ ml/cm H_2O	$Gf(l)$ (l/s)/cm H_2O
Expected value:	7.3	0.034
Initial investigation:	3.7	0.031
Reinvestigation:	0.53	0.004

heart failure during obstructive airway diseases. CPAP treatment without intubation seems to be an efficient and less harmful alternative to IPPV. During CPAP breathing the infection may be cured and surgical intervention may be delayed. During

such therapy repeated measurements of pulmonary mechanics could be of diagnostic and prognostic value. The face chamber is thus useful both as a therapeutical and a diagnostic tool.

GENERAL DISCUSSION

As pulmonary disease is one of the most frequent causes of illness in infancy the need of specific and sensitive methods for pulmonary investigations is obvious. Earlier described methods for studies of pulmonary mechanics have several disadvantages discussed above and most of them cannot be used in clinical routine investigations. The presented method fulfils reasonable demands on a safe and reliable method for such studies in infancy.

The method was proved to provide valuable information in the investigation of diseased infants. It could be used as a prognostic tool for the evaluation of infants with previous pulmonary diseases. Such studies can give information on the nature of the pulmonary malfunction with great use for decisions on therapy. The method can also be used for diagnosis of pulmonary or cardiac disease with obscure pulmonary symptoms. Evaluation of different therapeutical approaches to pulmonary disease is possible. The effect of drugs on pulmonary mechanics can thus easily be studied (III). This method for a more objective information on pharmacological effects in human infants may also be of importance in severe forms of chronic pulmonary disease in infants e.g. bronchial asthma and cystic fibrosis, which usually give symptoms during infancy (26). An early

efficient evaluation of the lung function and possible effects of different drugs may be of great prognostic value. It is likely that many of these infants although clinically healthy during certain periods, nevertheless have subclinical signs of pulmonary malfunction, only detectable with specific methods, such as the one presented here.

With suitable modifications, described above, the method may well be applicable during the neonatal period with its various forms of pulmonary diseases. It may further be possible in the future to let the computer take over more of the analysis of the available data. When more experience has been gained on various breathing patterns, a more complete computerized analysis is possible.

The present method for studies of pulmonary mechanics demands a certain amount of basic technical resources, and the method must therefore at present be reserved for the very large hospitals where equipment and personal staff are adequate. It is felt that the costs of this type of investigations should not be grudged, since an efficient evaluation of the mechanical properties of the lungs will undoubtedly contribute to better prophylaxis and improved treatment of pulmonary disease of infancy.

SUMMARY

For clinical studies of pulmonary mechanics in infants a new method is presented. This includes:

- 1) Measurements at sleep without use of sedatives.
- 2) Standardized measurements at rest and during carbon dioxide induced hyperventilation.
- 3) Carefully controlled equipment with respect to safety and comfort for the infants, avoidance of phase lag between the oesophageal pressure and air flow signals, and elimination of the effects of transient pressure variations in the ambient pressure.
- 4) Computerized calculations on line from the pressure and flow signals.
- 5) Possibilities of studies of the breathing pattern from e.g. pressure-flow loops.

With the method, normal infants were studied and normal values on e.g. tidal volume, minute ventilation, dynamic compliance and "functional" pulmonary conductance are presented.

The method was found suitable for clinical routine studies of pulmonary mechanics during infancy, even during severe ventilatory insufficien-

cy. Two groups of infants were investigated: infants surviving severe neonatal respiratory insufficiency and infants with cardio-vascular left-to-right shunts.

The results from these studies indicate that the method can be used for diagnostic purposes, to obtain information of prognostic value, and as a tool for evaluation of the effect of different therapeutical approaches to pulmonary diseases in infants.

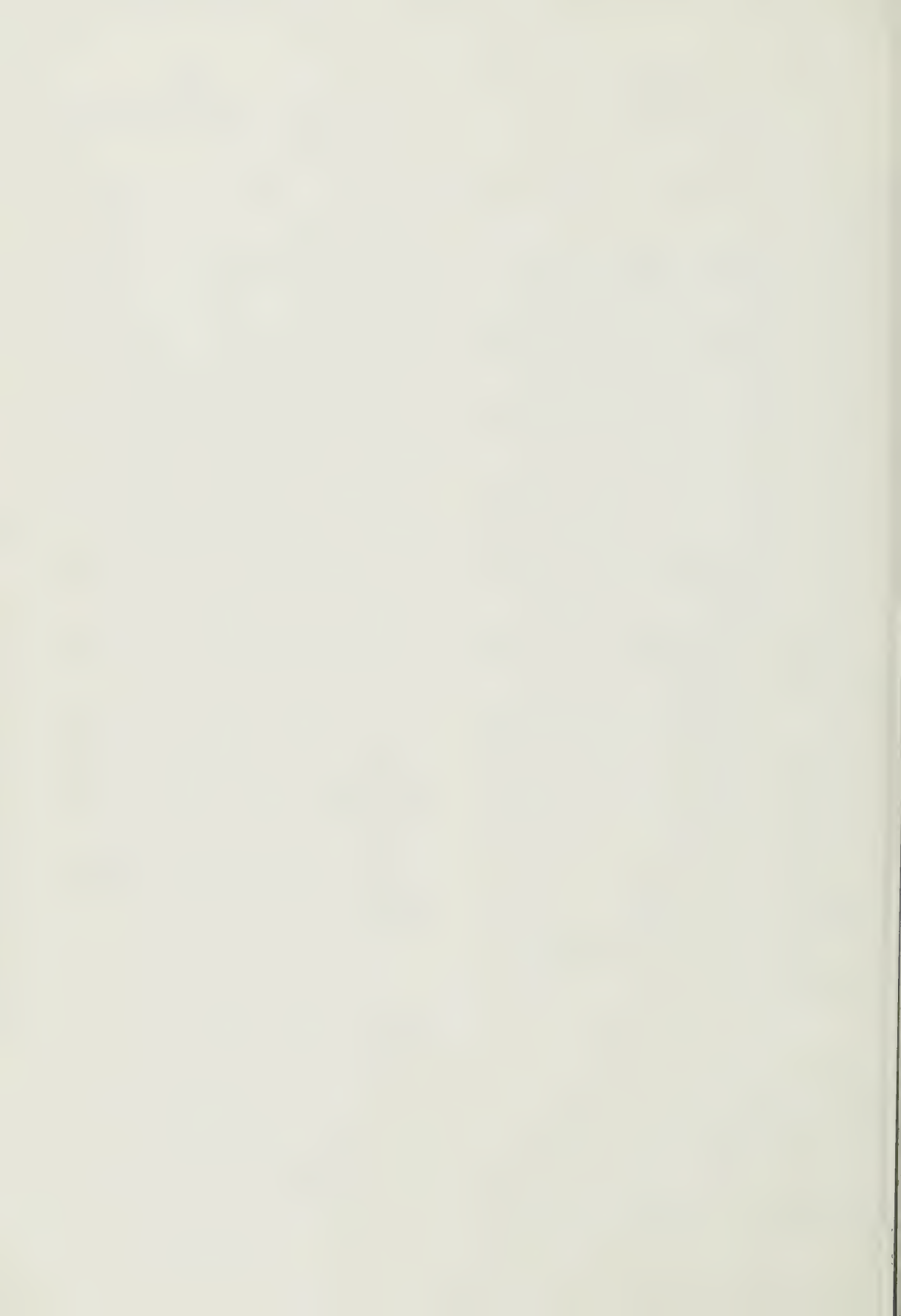
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